REMARKS

Claim 1 has been amended to clarify the meaning of "chemically defined" and to specify a minimal volume for fermentation. Support for the amendment with respect to "chemically defined" is found on page 5, for example, at lines 3-7 and at lines 14-23. Support for the specification of 10 m^3 is found on page 3, line 24 and at page 4, lines 32-36. No new matter has been added and entry of the amendment is respectfully requested.

The Invention

The invention resides in the description of a process for utilizing defined medium for production of antibiotics on an industrial scale. As is set forth in the specification, chemically defined media have been used in laboratory procedures in the past, but the problems presented by industrial scale fermentations are so different that it is not possible to extrapolate practices in the laboratory to the industrial environment. The amendment to the claims clarifies the magnitude of volume that is required for such an industrial scale fermentation.

The Rejections Under 35 U.S.C. § 112, Second Paragraph

Objection was made to the term "chemically defined medium"; it is believed that the amendment to the claims clarifies the meaning of this term. Applicants note that page 5 of the specification describes in detail what is meant by this requirement, and it is believed that the amendment to the claims, fully supported by the specification, provides this clarification. Chemically defined media utilize as carbon and nitrogen sources only materials which are of a composition that allows precise reproducibility of content; they are either pure chemicals such as glucose, or are mixtures of highly chemically related components such as vegetable oil. This is in contrast to ordinarily used sources for nutrients such as soybean meal, cottonseed meal, corn steep liquor, yeast extract and the like. It is believed that the ordinarily skilled artisan would

clearly understand the meaning both of "chemically defined" itself and the meaning of the term as now set forth in the claims. It is believed that this definition meets the requirements of the statute. Definition has been made as precisely as the language of the appropriate art will allow. (*Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F2d 1367, 231 USPQ 81 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987).)

Accordingly, this basis for rejection may be withdrawn with respect to the claims as amended.

The Rejection Under 35 U.S.C. § 102

Claims 1-4, 15-16, 19-20 and 36 were rejected as anticipated by Hogye, *et al.*

It is believed that the clarifying amendment to the claims overcomes this basis for rejection. There is nothing in the Hogye document which would lead one to conclude that the process described is conducted on an industrial scale, much less at a minimum volume of 10 m^3. It is noted that for anticipation to be found, all of the limitations of the claims must either be disclosed explicitly in the cited document, or, if inherently disclosed, the disclosure must be unambiguous and conclusive. Mere probabilities are not sufficient. (*Continental Can Co. USA, Inc. v. Monsanto Co.*, 948 F2d 1264, 20 USPQ2d 1746 (Fed. Cir. 1991).) Here, there is no indication whatsoever as to the scale of the fermentation in the cited document. Thus, the citation fails to meet the requirements for inherent anticipation as set forth by controlling precedent.

The Rejection Under 35 U.S.C. § 103

All claims were rejected as obvious over the combination of Hogye, *et al.*, in view of Bovenberg. Bovenberg is cited to show that 7-ADCA can be produced by fermentation; thus, in the Office's view, the combination of Bovenberg with Hogye would render obvious even any

claims which require production of adipoyl-7-ADCA (*i.e.*, claim 17) since Bovenberg putatively teaches this process. As applied to claims 5-8, the Office is of the view that the claim limitations are obvious permutations of the process taught by Hogye. The Office takes the view that Bovenberg teaches a process for the production of adipoyl-7-ADCA in a chemically defined medium.

Respectfully, the Office appears to have overlooked the nature of the invention. The amendment to the claim clarifies this. Neither Hogye nor Bovenberg teach the fermentation of any microorganism to produce any antibiotic on an industrial scale. Hogye is silent on the volume of fermentation, and it cannot be concluded that a volume of at least 10 m^3 would have been used. If one cannot come to this conclusion unequivocally, the disclosure of Hogye cannot be said to suggest the invention. The disclosure of Bovenberg is unequivocally dramatically less than a fermentation volume of 10 m^3; the fermentation volume as set forth in Example 1 is only 15 ml. This is exactly the type of laboratory fermentation distinguished by the applicants from their invention as described in the specification itself on page 3, beginning at line 8.

Accordingly, neither Hogye nor Bovenberg, alone or in combination, in any way suggest the process of claim 1 which requires a minimum volume of 10 m^3 in combination with a chemically defined medium. As claim 1 is not suggested, the putatively obvious variations set forth in claims 5-8 are not suggested either, nor is the subject matter of any of dependent claims suggested thereby. Accordingly, this basis for rejection may also be withdrawn.

CONCLUSION

The invention resides in the teaching that production of β-lactam antibiotics may be effected in a defined medium, not just on a laboratory scale, but also on an industrial scale. No document has been cited that either discloses or suggests this combination of defined medium

believed that claims 1-8, 15-16, 19-20 and 36-37 are in a position for allowance and passage of these claims to issue is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 246152012710.

Respectfully submitted,

Dated: May 20, 2002

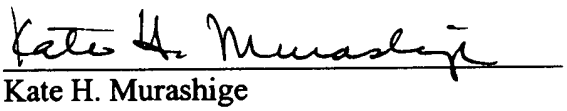
By: 

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EXHIBIT A. - VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

1. (Twice amended) A process for the production of a β-lactam, comprising the steps of:

a) fermenting on [an industrial] a volume scale of at least 10 m^3, a microbial strain that produces a β-lactam in a fermentation medium which [is a] utilizes only chemically defined [medium consisting of chemically defined constituents] components as carbon and nitrogen sources and contains no complex raw materials, and

b) recovering the β-lactam from the fermentation medium.

strain in medium

3. (Twice amended) The process of claim 1, wherein the chemically defined [constituents] components comprise a carbon source selected from the group consisting of glucose, lactose, fructose, sucrose, a maltodextrin, starch inulin, glycerol, a vegetable oil, a hydrocarbon, an alcohol, an organic acid, and/or a nitrogen source selected from the group consisting of urea, ammonia, nitrate, an ammonium salt and an amino acid.